

WHAT IS CLAIMED IS:

1. A method for identifying a non-competitive peptide which inhibits the activity of a cytokine receptor, said method comprising selecting a candidate peptide containing from about 7 to about 20 amino acids derived from a flexible region of the receptor, and determining the ability of the candidate peptide to inhibit the oligomerization and/or activity of the receptor by measuring a biological activity of said receptor in the absence or presence of the candidate peptide, wherein a non-competitive peptide is selected when the activity of the receptor is measurably lower in the presence of the candidate peptide as compared to in the absence thereof.

2. The method of claim 1, wherein the candidate peptide contains at least one amino acid which is not present in the region of the receptor from which it originates, and wherein said at least one amino acid does not significantly affect the antagonistic activity of the candidate peptide.

3. The method of claim 1, wherein said compound is protein resistant.

4. The method of claim 1, wherein the receptor is human VEGFR and the peptide is derived from a flexible region of human VEGFR which maps to residues selected from the group consisting of:

a) residues 320-350;

b) residues 350-400;

c) residues 400-440;

d) residues 481-565;

e) residues 640-685; and

d) residues 745-770.

5. The method of claim 1, wherein the receptor is human interleukin-1 receptor (IL-1R α) and the peptide is derived from a flexible region of human IL-1R which maps to residues selected from the group consisting of:

a) residues 181-200;

b) residues 209-240; and

c) residues 320-341.

6. The method of claim 1, wherein the receptor is human interleukin-1 receptor (IL-1R) accessory protein and the peptide is derived from a flexible region of IL-1R accessory protein which maps to residues selected from the group consisting of:

a) residues 115-160;

b) residues 170-266;

c) residues 200-215;

d) residues 275-295;

e) residues 300-315; and

f) residues 330-370.

7. The method of claim 1, wherein the receptor is human Insulin-like growth factor 1 receptor (IGF-1R) and the peptide is derived from a flexible region of human IGF-1R which maps to residues selected from the group consisting of:

a) residues 320-335;

- b) residues 487-527;
- c) residues 595-620;
- d) residues 660-690;
- e) residues 725-740;
- f) residues 780-799;
- g) residues 820-840; and
- h) residues 917-947.

8. The method of claim 1, wherein the receptor is human interleukin-4 receptor (IL-4R) and the peptide is derived from a flexible region of human IL-4R which maps to residues selected from the group consisting of:

- a) residues 112-125;
- b) residues 125-216; and
- c) residues 210-240.

9. The method of claim 1, wherein the receptor is human EGFR and the peptide is derived from a flexible region of human EGFR which maps to residues selected from the group consisting of:

- a) residues 335-345;
- b) residues 495-515; and
- c) residues 640-650.

10. The method of claim 1, wherein the receptor is human GHR and the peptide is derived from a flexible region of human GHR which maps to residues selected from the group consisting of:

a) residues 160-240; and

b) residues 250-270.

11. A method for identifying a peptidomimetic which inhibits the activity of a cytokine receptor, said method comprising the steps of selecting a non-peptidyl compound of a cytokine receptor antagonist peptide containing from about 7 to about 20 amino acids, derived from a flexible region of said cytokine receptor, and determining the ability of said peptidomimetic to inhibit the activity of the receptor.

12. A non-competitive extracellular cytokine receptor antagonist, wherein said antagonist is a peptide containing from about 7 to about 20 amino-acids derived from a flexible region of said cytokine receptor.

13. The antagonist of claim 12, wherein said cytokine receptor is human VEGFR and said peptide is derived from a VEGFR region selected from the group consisting of

a) residues 320-350;

b) residues 350-400;

c) residues 400-440;

d) residues 481-565;

e) residues 640-685; and

f) residues 745-770.

14. The antagonist of claim 12, wherein said cytokine receptor is human interleukin-1 receptor (IL-1R) accessory protein and said peptide is derived from a IL-1R accessory protein region selected from the group consisting of

- a) residues 115-160;
- b) residues 170-266;
- c) residues 200-215;
- d) residues 275-295;
- e) residues 300-315; and
- f) residues 330-370.

15. The antagonist of claim 12, wherein said cytokine receptor is human IL-1R and said peptide is derived from a human IL-1R region selected from the group consisting of

- a) residues 181-200;
- b) residues 209-240; and
- c) residues 320-341.

16. The antagonist of claim 12, wherein said cytokine receptor is human IGF1R and said peptide is derived from a human IGF-1R region selected from the group consisting of

- a) residues 320-335;
- b) residues 487-527;

- c) residues 595-620;
- d) residues 660-690;
- e) residues 725-740;
- f) residues 780-799;
- g) residues 820-840; and
- h) residues 917-947.

17. The antagonist of claim 12, wherein said cytokine receptor is human IL-4R and said peptide is derived from a IL-4R region selected from the group consisting of

- a) residues 112-125;
- b) residues 125-216; and
- c) residues 210-240.

18. A method of inhibiting human VEGFR activity comprising targeting VEGFR with an antagonist of claim 13.

19. A method of inhibiting human IL-1RacP activity comprising targeting IL-1R accessory protein with a peptide of claim 14.

20. A method of inhibiting human IL-1R activity comprising targeting IL-1R with a peptide of claim 15.

21. A method of inhibiting human IGF-1R activity comprising targeting IG1R with a peptide of claim 16.

22. A method of inhibiting human IL-4R activity comprising targeting IL-4R with a peptide of claim 17.

23. The method of claim 18, wherein said antagonist is a peptide having a sequence selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2 and SEQ ID NO. 3 of VEGFR.

24. The method of claim 19 wherein said antagonist is a peptide having a sequence selected from the group consisting of SEQ ID NO. 50, SEQ ID NO: 52 and SEQ ID NO: 53 of IL-1R.

25. The method of claim 21 wherein said antagonist is a peptide having a sequence selected from the group consisting of SEQ ID NO. 11, SEQ ID NO. 14 and SEQ ID NO. 16 of IGF-1R.

26. The method of claim 22 wherein said antagonist is a peptide having a sequence selected from the group consisting of SEQ ID NO. 35, SEQ ID NO. 36, SEQ ID NO. 37, SEQ ID NO. 38 and SEQ ID NO. 39 of IL-4R.

27. The method of claim 18 wherein said antagonist is peptidomimetic of a peptide having a sequence selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2 and SEQ ID NO. 3 of VEGFR.

28. The method of claim 19 wherein said antagonist is peptidomimetic of a peptide having a sequence selected from the group consisting of SEQ ID NO. 50, SEQ ID NO: 52 and SEQ ID NO: 53 of IL-1R.

29. The method of claim 21 wherein said antagonist is peptidomimetic of a peptide having a sequence selected from the group consisting of SEQ ID NO. 11, SEQ ID NO. 14 and SEQ ID NO.16 of IGF-1R.

30. The method of claim 22 wherein said antagonist is peptidomimetic of a peptide having a sequence selected from the group consisting of SEQ ID NO. 35, SEQ ID NO. 36, SEQ ID NO. 37, SEQ ID NO. 38 and SEQ ID NO. 39 of IL-4R.

31. A method for treating a disease or condition in an animal said disease or condition being characterized by an abnormality in a signal transduction pathway, involving cytokine receptor activity, comprising the step of administering to said animal a therapeutically effective amount of a cytokine receptor subfragment peptide or derivative thereof under conditions effective to ameliorate the cytokine receptor mediated signaling, wherein said cytokine receptor subfragment peptide or derivative thereof is an antagonist of claim 12.

32. A pharmaceutical composition for treating a disease or condition in an animal characterized by an abnormality in a signal transduction pathway involving cytokine receptor activity comprising an effective amount of a cytokine receptor antagonist subfragment peptide or derivative thereof together with a pharmaceutically acceptable carrier, wherein said cytokine receptor subfragment peptide or derivative thereof is an antagonist of claim 12.

33. A method for identifying a non-competitive peptide which acts as a cytokine receptor agonist, said method comprising the steps of selecting a candidate peptide containing from about 7 to about 20 amino acids derived from a flexible region of the receptor, and determining the ability of the candidate peptide to inhibit the oligomerization and/or activity of the receptor by measuring a biological activity of said receptor in the absence or presence of the candidate peptide, wherein a non-competitive peptide is selected when the activity of the receptor is measurably higher in the presence of the candidate peptide as compared to in the absence thereof.

34. The method of claim 33, wherein the candidate peptide contains at least one amino acid which is not present in the region of the receptor from which it originates, and wherein said at least one amino acid does not significantly affect the agonistic activity of the candidate peptide.

35. The method of claim 33, wherein said compound is protein resistant.

36. A method for identifying a peptidomimetic which activates the activity of a cytokine receptor, said method comprising the steps of selecting a non-peptidyl compound of a cytokine receptor agonist peptide containing from about 7 to about 20 amino acids, derived from a flexible region of said cytokine receptor, and determining the ability of said peptidomimetic to enhance the activity of the cytokine receptor.

37. A non-competitive extracellular cytokine receptor agonist, wherein said agonist is a peptide containing from about 7 to about 20 amino-acids derived from a flexible region of said cytokine receptor.